Updates in Interventional Cardiology and Guidelines

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Disclosures

No Conflicts of Interest

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TOPICS

- Anti Platelet Therapy
- Updates on Bioresorbable Scaffolds
- Updates on TAVR
  (Transcatheter Aortic Valve Replacement)
**Updates in Interventional Cardiology and Guidelines**

- Major Society Guideline updates 2016-2017
- Clinical Trials Published 2016-2017
- Regulatory News and Events

**Strength of Guideline Recommendations**

**TOPICS**

- Anti Platelet Therapy
- Updates on Bioresorbable Scaffolds
- Updates on TAVR (Transcatheter Aortic Valve Replacement)
# Antiplatelet Agents

<table>
<thead>
<tr>
<th>Indication</th>
<th>Aspirin</th>
<th>Clopidogrel (Plavix)</th>
<th>Prasugrel (Effient)</th>
<th>Ticagrelor (Brilinta)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS Post PCI Stroke</td>
<td>ACS Post PCI Stroke</td>
<td>ACS Post PCI Stroke</td>
<td>ACS Post PCI Stroke</td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td>81 mg DAILY</td>
<td>300-600 mg DAILY</td>
<td>60 mg</td>
<td>180 mg</td>
</tr>
<tr>
<td>Class</td>
<td>NSAID</td>
<td>2nd gen thiopyridine (PRODRUG)</td>
<td>2nd gen thiopyridine (PRODRUG)</td>
<td>CTPI</td>
</tr>
<tr>
<td>Mechanism</td>
<td>IRREVERSIBLE COX-1</td>
<td>IRREVERSIBLE</td>
<td>IRREVERSIBLE</td>
<td>REVERSIBLE</td>
</tr>
<tr>
<td>Peak Effect</td>
<td>1-3 hours</td>
<td>6 hours</td>
<td>4 hours</td>
<td>2 hours</td>
</tr>
<tr>
<td>CYP Metabolism</td>
<td>NA</td>
<td>2C19</td>
<td>3A4</td>
<td>3A4/5</td>
</tr>
</tbody>
</table>

## Aspirin Dosing in Patients with CAD

- Higher doses of aspirin are associated with bleeding and no increased anti-ischemic benefit.
- When used with ticagrelor (Brilinta), aspirin doses of >100 mg are contraindicated.
According to US Guidelines, how long should patients be on Dual Antiplatelet Therapy (DAPT) after PCI with a Drug Eluting Stent?

A. 3 months  
B. 6 months  
C. 12 months  
D. It depends on the indication for PCI  
E. Call a cardiology consult

Duration of Dual Antiplatelet Therapy (DAPT)

- Duration of DAPT depends on:
  - Underlying condition  
  - Treatment provided

Stable Ischemic Heart Disease (SIHD)  
Acute Coronary Syndromes (ACS)

Duration of Dual Antiplatelet Therapy (DAPT) in Patients with ACS

Stopping early at 6 months
Duration of Dual Antiplatelet Therapy (DAPT) in Patients with SIHD

Stable Ischemic Heart Disease (SIHD)

- PCI with Bare Metal Stent (BMS) 1 MONTH
- PCI with Drug Eluting Stent (DES) 6 MONTHS

Stopping early at 3 months

When should DAPT therapy be continued for LONGER Duration?

Risk of Ischemia
- Increased risk of stent thrombosis
- ACS presentation
- Diabetes mellitus
- Left ventricular ejection fraction <40%
- Prior generation drug eluting stent
- Stent underdeployment
- Small stent diameter
- Greater stent length
- In-stent restenosis

Risk of Bleeding
- History of prior bleeding
- Oral anticoagulant therapy
- Female sex
- Advanced age
- Low body weight
- CKD
- Diabetes mellitus
- Anemia
- Chronic renal or HSCT therapy

The DAPT Score can guide risk / benefit of longer therapy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≤ 75 y</td>
<td>-2</td>
</tr>
<tr>
<td>Age 75 to &lt;75 y</td>
<td>-1</td>
</tr>
<tr>
<td>Age ≥ 85 y</td>
<td>0</td>
</tr>
<tr>
<td>Current cigarette smoker</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>MI at presentation</td>
<td>1</td>
</tr>
<tr>
<td>Prior PCI or prior MI</td>
<td>1</td>
</tr>
<tr>
<td>Stent diameter &lt;3 mm</td>
<td>1</td>
</tr>
<tr>
<td>Radiation-eluting stent</td>
<td>1</td>
</tr>
<tr>
<td>GFR or LVEF &lt;30%</td>
<td>2</td>
</tr>
<tr>
<td>Saphenous vein graft PCI</td>
<td>2</td>
</tr>
</tbody>
</table>
Which P2Y12 Agent should I recommend?

For Medically Managed ACS

Recommended over

For ACS with PCI

Recommended over

What's the update on triple therapy?

For patients who require triple therapy:
- Use Coumadin (keep INR at low end of range)
- Use Clopidogrel
- Use low dose aspirin
- Consider PPI

65 yo man underwent PCI with a drug eluting stent to the LAD 2 months ago for stable angina. He now has severe knee osteoarthritis and is asking you when he can have surgery. How long after his stent should he wait?

A. 1 month
B. 3 months
C. 6 months
D. 12 months
E. He should be managed medically indefinitely
During perioperative period:
- Continue aspirin if possible
- Restart P2Y12 as soon as possible

Key Points Regarding DAPT (1/2)
- Dose of Aspirin for all patients is **81 mg daily**
- Duration of DAPT:
  - ACS Patients: **1 YEAR for ALL** (with/without stent)
  - SIND Patients:
    - Drug Eluting Stent (DES): **6 MONTHS**
    - Bare Metal Stent (BMS): **1 MONTH**
- Stopping Early:
  - DAPT could be stopped **3 months** after DES for high bleeding risk patients
- Longer Therapy:
  - Risk benefit between bleeding and ischemia
  - DAPT score can be helpful
Key Points Regarding DAPT (2/2)

- **Choice of Agents:**
  - Medical Management of ACS: Ticagrelor > Plavix
  - PCI in ACS: Ticagrelor or Prasugrel > Plavix
  - Do NOT USE Prasugrel if history of stroke or TIA
- **Triple Therapy:**
  - Short Duration
  - Use clopidogrel/coumadin
  - Target INR 2-2.5
  - Use PPI
- **Timing of Non-Cardiac Surgery:**
  - Ideally > 1 month after BMS, 6 months after DES
  - Continue Aspirin if possible

Updates in Interventional Cardiology and Guidelines

**TOPICS**
- Anti Platelet Therapy
- Updates on Bioresorbable Scaffolds
- Updates on TAVR (Transcatheter Aortic Valve Replacement)

Limitations of current Metallic Stents

- The standard of care for PCI for the last decade has been metallic stents
  - Bare Metal or Drug Eluting

- Metallic scaffolds have **disadvantages:**
  - Rigid metallic cages hamper vasomotion
  - Development of neoatherosclerosis
    - Risk of stent thrombosis 0.1-0.2%/yr
    - Risk of repeat revascularization 2-3%/yr
  - Delayed stent endothelialization
  - Permanent implant cannot be removed
Bioresorbable Vascular Scaffold (BVS): ABSORB

- NO Permanent Implant!
  - Allows for restoration of vessel function (theoretical benefit)
  - Maintain option for future surgery (CABG)
  - Fewer permanent layers of metal in patients requiring treatment for stent restenosis (ISR)

**ABSORB GT1 (Abbott Vascular)**

- Absorbable polymer, poly(L-lactide) (PLLA)
- Thin coating of the absorbable polymer, poly(D,L-lactide) (PDLLA) with everolimus drug coating

A 52 yo M has ongoing CCS Class III stable angina despite maximal medical therapy. Coronary angiography demonstrates a 90% focal RCA lesion. He is considering PCI and requests your opinion regarding a bioresorbable stent. What do you tell him?

A. "It’s the latest and greatest, go for it"
B. "The risks and benefits appear to be similar to current metallic stents."
C. "Steer Clear, at least for now!"

**ABSORB III Trial**

- 2008 patients with stable or unstable angina randomly assigned in a 2:1 ratio to receive Absorb or an everolimus-eluting cobalt-chromium (Xience) stent
- Primary end point: target-lesion failure (cardiac death, target-vessel myocardial infarction, or ischemia-driven target-lesion revascularization) at 1 year

*The NEW ENGLAND JOURNAL of MEDICINE*

Everolimus-Eluting Bioresorbable Scaffolds for Coronary Artery Disease
ABSORB III Results

- Target lesion failure non-inferior for ABSORB
- No difference in cardiac Death at 1 (0.8% vs 0.7%, p=0.29)
- Signal for increase in stent thrombosis at 1 year (1.5% vs 0.7%, p=0.13)

Follow up data shows higher Stent Thrombosis (March 2017)

AIDA Trial

- 1845 patients undergoing PCI randomly assigned to receive either a bioresorbable vascular scaffold or a metallic stent.
- Primary end point: Target-vessel failure (a composite of cardiac death, target-vessel myocardial infarction, or target-vessel revascularization) through 2 years.
- The data and safety monitoring board recommended early reporting of the study results because of safety concerns.

AIDA Results – Target Lesion Failure

- Target lesion failure non-inferior for ABSORB
Definite Stent Thrombosis significantly higher for BVS
- 27 events vs 5!

The fate of ABSORB

Results from 1 year follow-up of ABSORB shown at American College of Cardiology Meeting (3/2017):
- Target Lesion Failure: 11.0% vs 7.9% (significant)
- Target Vessel Myocardial Infarction: 7.3% vs 4.9% (p=0.04)
- Stent Thrombosis: 1.9 vs 0.8%

Limited to Registry Use in the European Market (Registry only use allowed)
Key Points Regarding BVS

- Data through 2 years demonstrate a significantly higher risk of stent thrombosis with ABSORB
- FDA warning letter issued 3/2017
- ABSORB limited to registry use in the EU (3/2017)

Bioresorbable Vascular Scaffolds May Not Be Ready for Primetime

Updates in Interventional Cardiology and Guidelines

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- Updates on Bioresorbable Scaffolds
- Updates on TAVR (Transcatheter Aortic Valve Replacement)

Aortic Stenosis

- Degree of Aortic Stenosis is determined by Echocardiography
- Symptoms are key!

AHA Guidelines for Severity of Aortic Stenosis

<table>
<thead>
<tr>
<th>Severity</th>
<th>Valve Area (cm²)</th>
<th>Maximum Aortic Velocity (mmHg)</th>
<th>Mean Pressure Gradient (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>1.5-2</td>
<td>2.5-3.0</td>
<td>&lt; 25</td>
</tr>
<tr>
<td>Moderate</td>
<td>1.0-1.5</td>
<td>3.0-4.0</td>
<td>25-40</td>
</tr>
<tr>
<td>Severe</td>
<td>0.6-1.0</td>
<td>&gt;4.0</td>
<td>&gt;40</td>
</tr>
<tr>
<td>Critical</td>
<td>&lt; 0.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Valve replacement indicated for Stage C2 and D Aortic Stenosis – Progression of Disease

Intervening on patients with severe symptomatic AS improves survival

Survival Without Treatment is Poor

5 year survival of breast cancer, lung cancer, prostate cancer, ovarian cancer and severe inoperable aortic stenosis
2. Iung B et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease. European Heart Journal 2003;24:1231-1243 (*includes both Aortic Stenosis and Mitral Regurgitation patients)

High Risk Patients Previously Untreated

TAVR Approved by FDA in US in 2011

Multiple TAVR Valve Platforms have been developed

Two valves commercially available in US

- Edwards Sapien S3
  - Bovine pericardial tissue
  - Stainless steel frame
  - PET skirt
  - Transfemoral, transapical, transaortic delivery
  - Balloon expandable system

- Medtronic CoreValve
  - Transfemoral or subclavian delivery
  - Repositionable, self-expanding system
Inoperable PARTNER Cohort
Primary Endpoint: All-Cause Mortality

Leon et al, NEJM 2010; 363:1597-1607

Primary Endpoint: All-Cause Mortality at 1 Year

CoreValve US Pivotal Trial High Risk Study 3-Year Outcomes (All Cause Mortality)

Lower all cause mortality for TAVR group
CoreValve US Pivotal Trial High Risk Study 3-Year Outcomes (Stroke)

- Lower stroke for TAVR group

CoreValve US Pivotal Trial High Risk Study 3-Year Outcomes (Hemodynamics)

- Higher valve area and lower gradients for TAVR

TAVR for High Risk and Inoperable Patients

KEY POINT:

For high risk and inoperable patients, TAVR is better than medical therapy and equivalent or better than surgery.
**TAVR has been studied across the risk spectrum of patients**

- Two-thirds of patients will remain optimal surgical candidates.

**Low RISK**
- STS PROM < 4%
- 30-Day Mortality < 2-4%

**Intermediate RISK**
- PARTNER II
- SURTAVI
- STS ≥ 4

**High RISK**
- PARTNER A
- CoreValve High Risk
- PARTNER B
- CoreValve Extreme Risk

**Surgical Aortic Valve Replacements**
- 70-90,000 yearly
- Inoperable 20-50K

**Pivotal Trials for Intermediate Risk TAVR**

**SURTAVI Trial (NEJM 2017)**
- TAVR with self-expanding valve vs surgery (SAVR)
- Intermediate Risk Patients (STS Score 4-8)
- Severe Symptomatic Aortic Stenosis
- Randomized Controlled Non-Inferiority Trial
- Primary Endpoint: Composite of Death or disabling stroke at 24 months
- 1746 patients randomized (1660 underwent valve replacement)
- 87 centers

**The NEW ENGLAND JOURNAL OF MEDICINE**

Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients

SURTAVI Trial (NEJM 2017) - Results

- Primary outcome met!
- Death/Stroke at 24 months: 12.6% vs 14%

Mortality similar (11.4 vs. 11.6%)
Stroke numerically lower in TAVR (2.6% vs. 4.5%)

As with other TAVR studies:
- Valve area is larger
- Valve gradients are lower
The Tradeoff is higher rates of vascular complication and pacemaker implantation

Point 1: Risk Evaluation Should Include STS Score, Frailty and Comorbidities

**ACC Clinical Document**

2017 ACC Expert Consensus Decision Pathway for Transcatheter Aortic Valve Replacement in the Management of Adults With Aortic Stenosis

A Report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents

2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

**SURTAVI Trial (NEJM 2017) - Results**

Table 1: Procedure-Related Complications at 30 Days (Modified intention-to-treat Population)."  

<table>
<thead>
<tr>
<th>Complication</th>
<th>TXMV (N=964)</th>
<th>Surgery (N=794)</th>
<th>95% Confidence Interval for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life-threatening or major bleeding — %</td>
<td>3.2</td>
<td>3.5</td>
<td>-3.2 to 5.5</td>
</tr>
<tr>
<td>Transfusion of red cells — no. (%)</td>
<td>764 (79.7)</td>
<td>640 (81.3)</td>
<td>18.4 to 23.5</td>
</tr>
<tr>
<td>3 units</td>
<td>29 (3.0)</td>
<td>96 (12.1)</td>
<td>-10.5 to -3.1</td>
</tr>
<tr>
<td>2 to 4 units</td>
<td>48 (5.0)</td>
<td>156 (20.1)</td>
<td>-16.5 to -5.0</td>
</tr>
<tr>
<td>5+ units</td>
<td>11 (1.1)</td>
<td>100 (12.7)</td>
<td>-11.7 to -6.5</td>
</tr>
<tr>
<td>Acute kidney injury stage 2 or 3 — %</td>
<td>1.7</td>
<td>4.4</td>
<td>-4.4 to -2.8</td>
</tr>
<tr>
<td>Coronary artery obstruction — %</td>
<td>0.2</td>
<td>0.0</td>
<td>-0.2 to 0.8</td>
</tr>
<tr>
<td>Major vascular complication — %</td>
<td>69</td>
<td>3.4</td>
<td>3.4 to 6.7</td>
</tr>
<tr>
<td>Cardiac perforation — %</td>
<td>1.1</td>
<td>0.0</td>
<td>-0.2 to 0.8</td>
</tr>
<tr>
<td>Cardiac shock — %</td>
<td>1.1</td>
<td>3.8</td>
<td>-4.2 to 1.8</td>
</tr>
<tr>
<td>Permanent pacemaker implantation — %</td>
<td>2.5</td>
<td>5.2</td>
<td>19.9 to 22.7</td>
</tr>
</tbody>
</table>

*The Tradeoff is higher rates of vascular complication and pacemaker implantation*
Point 2: Intermediate risk patients are now indicated for TAVR (IIa)

TAVR indicated for intermediate, high and prohibitive risk patients

Point 3: Long-Term Follow-up for TAVR Patients Defined

Point 4: Endocarditis prophylaxis after TAVR

Patients with Transcatheter valves should receive endocarditis prophylaxis prior to dental procedures

- Infective Endocarditis (IE) has been reported to occur after TAVR at rates equal to or exceeding those associated with surgical aortic valve replacement (AVR)
- TAVR IE is associated with a high 1-year mortality rate of 75%


Infective Endocarditis (IE) has been reported to occur after TAVR at rates equal to or exceeding those associated with surgical aortic valve replacement (AVR)
Point 5: Anticoagulation after TAVR

Anticoagulation with a VKA to achieve an INR of 2.5 may be reasonable for at least 3 months after TAVR in patients at low risk of bleeding

- Studies have shown that valve thrombosis may develop in patients after TAVR, as assessed by CT scanning (7-40%).
- Valve thrombosis occurs in patients who received antiplatelet therapy alone but not in patients who were treated with VKA.

Point 6: Antiplatelet Therapy after TAVR

Clopidogrel 75 mg daily may be reasonable for the first 6 months after TAVR in addition to lifelong aspirin 75 mg to 100 mg daily.

Key Points Regarding TAVR (1/2)

- Risk assessment for patients should include STS Score, Frailty and Comorbidities
- For Patients with Symptomatic Severe Aortic Stenosis (Stage D) whose risk for surgical valve replacement is:
  - Inoperable: TAVR has a CLASS I indication
  - High Risk: TAVR has a CLASS I indication
  - Intermediate Risk: TAVR is reasonable (CLASS IIa)
    - Risks for pacemaker placement are high
    - Risk for vascular complications remain elevated
  - Low Risk: Surgery is Preferred
Key Points Regarding TAVR (2/2)

- Patients with a TAVR valve should receive prophylaxis for endocarditis (CLASS IIa)
- Anticoagulation with a VKA antagonist (Coumadin) may be reasonable for 3 months after TAVR to prevent valve thrombus (CLASS IIb)
- Clopidogrel 75 mg daily for 6 months and ASA 81 mg daily for life may be reasonable after TAVR (CLASS IIb)

What Have We Learned?

Dual Antiplatelet Therapy
- Duration of DAPT after ACS and PCI
- Choice of Antiplatet Agents
- An Approach to Triple therapy with Anticoagulation and DAPT
- Timing of Non Cardiac Surgery after PCI

BioResorbable Stents
- Bioresorbable Stents are not ready for primetime!

What Have We Learned?

Transcatheter Aortic Valve Replacement (TAVR)
- TAVR is now indicated for intermediate risk patients with Symptomatic Severe Aortic Stenosis
  - Rates of pacemaker implantation and vascular injury are higher with TAVR compared to surgery
- Patients with TAVR valves should receive endocarditis prophylaxis
- Antiplatelet agents and VK antagonists may be considered for use after TAVR implantation
References

Guidelines


Trials


Thank You!

Questions / Final syllabus:

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